

Appl. No. 10/718,107
Response dated September 17, 2007
Reply to Office Action of April 17, 2007

REMARKS

The claims have been amended. Claims 48, 86 and 116 have been cancelled. No new matter has been added to the application.

Claim 48 was rejected under 35 U.S.C. §101 as claiming the same invention as that of claim 1 of prior US Patent No. 6,821,961. Claims 48, 55, 85, 91, 116, 119 and 124 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1, 4-6 and 9 of US Patent No. 6,821,961. Claims 48, 55, 85-86, 91, 116-117, 119 and 194 were rejected under 35 U.S.C. §103(a) as being unpatentable over Alemany, et al. (US Patent No. 5,798,348) in view of Zhu, et al. (Carcinogenesis, vol. 19, no. 1, pp 1-27, 1998). Claims 48, 55, 85, 91 116 and 119 were rejected under 35 U.S.C. § 102(b) as being anticipated by Alemany, et al. (US Patent No. 5,798,348). Claims 48, 55, 85-86, 91, 116-117, 119 and 194 were rejected under 35 U.S.C. §112, first paragraph, because the specification does not reasonably provide enablement for using substantially pure 2-hydroxyestrone eicosenoate. Claims 48, 55, 85-86, 91, 116-117, 119 and 194 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Rejection under 35 U.S.C. §101

Applicant has cancelled claim 48. Applicant believes that this rejection is now moot and the remaining claims are allowable.

Rejection under non-statutory double patenting

Applicant has filed, contemporaneously herewith, a terminal disclaimer so that the term of this patent does not exceed that of US Patent No. 6,821,961. Applicant believes that this rejection is now moot and the remaining claims are allowable.

Rejection under 35 U.S.C. §112, first and second paragraphs

Applicant respectfully traverses these rejections.

Applicant respectfully submits that the language “substantially pure” is sufficiently definite to one skilled in the art. Further, there is a reference in the examples to 80% purity and 81% purity at page 12, lines 23-26. There is also a reference to 98% purity at page 6, lines 30-32. The purity of 2 hydroxyestrone is discussed at page 49, lines 21-23. Applicant believes that

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the claims are allowable.

Rejection under 35 U.S.C. §102(b)

The Examiner alleges that Claims 48, 55, 85, 91 116 and 119 are anticipated by the Alemany reference. Applicant respectfully disagrees with this rejection.

Applicant has amended the claims to specify that the fatty acid contains at least 20 carbon atoms. This finds support throughout the application as filed, including at page 3, line 21; page 5, lines 9, 12-15, 22; page 10, lines 27-30 and Examples 4-7. Applicant distinguishes the Alemany reference in the specification at page 8, lines 9-26, and page 9, lines 8-14. Alemany requires 18 or less carbon molecules. The applicant prefers compounds with more than 18 carbon molecules. The applicant has found that the higher carbon molecule compounds are more active and thus more effective for weight loss.

Applicant has amended the claims to specify that the estrogen derivative is a 2 hydroxy derivative. This finds support in Examples 8-12 of the specification as filed. The 2-hydroxy molecule is of particular importance. The estrogen molecule, by itself in a biological system, has been reported to have positive carcinogenic properties. With a hydroxyl group in position 2, the molecule is believed to be anti-carcinogenic. If the hydroxyl group is in position 16, the resulting compound is believed to be more carcinogenic than the unmodified molecule. Examples 8-12 show the significance of the 2-hydroxy molecule. None of the prior art references cited in the Office Action make any mention of such derivatives.

Rejection under 35 U.S.C. §103(a)

The Examiner alleges that it would be obvious to combine Alemany and Zhu et al. to arrive at applicant's invention as claimed in Claims 48, 55, 85-86, 91, 116-117, 119 and 194. Applicant respectfully disagrees with this rejection.

Alemany teaches against applicant's inventions as claimed (see discussion above). Applicant respectfully disagrees with the Examiner that "Zhu et al. suggest 2-hydroxyestrone is a major metabolite of estrone". Zhu et al. lists 2-hydroxyestrone as one of many metabolites of estrone (see table 1 of Zhu et al.).

Applicant asserts that Zhu, et al. suggests that "certain estrogen metabolites may function as chemical mediators or as secondary hormones with **unique functions**." Zhu, et al.

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(Carcinogenesis, vol. 19, no. 1, pp.16-17, emphasis added). Zhu, et al. specifically points out that estrogen metabolism “not only alters the intensity of estrogen action but may also alter its profile of physiological effects,” that this is an “underexplored area in need of more attention” and that further research “may lead to an enhanced understanding of estrogen action.” Zhu, et al. (Carcinogenesis, vol. 19, no. 1, p. 17).

With regard to 2-hydroxyestradiol, Zhu et al. reports that it is of “considerable interest that there are large interindividual differences in the 2-hydroxylation of estradiol or estrone by human liver samples and these inter-individual differences may be reflected by person-to-person differences in estrogen action in different individuals.” Zhu, et al. (Carcinogenesis, vol. 19, no. 1, p. 3). Zhu et al. continues that it will be of “interest **to identify** the cytochrome P450 isoforms that have high activity for the peroxidatic formation of catechol estrogens in liver or estrogen target tissues, and **to ascertain the physiological significance** of this peroxidatic pathway *in vivo*” and “the concentrations of unconjugated 2-hydroxyestradiol and 2-hydroxyestrone metabolites are very low in the systemic circulation and in several tissues, which is probably due to rapid conjugative metabolism followed by urinary excretion.” Zhu et al. (Carcinogenesis, vol. 19, no. 1, p. 4, emphasis added).

With regard to estrogen fatty acid esters, Zhu et al. suggests that it will be “**of considerable interest to advance our knowledge** on the formation, storage and, in particular, subsequent hydrolysis of estrogen-fatty acid esters” and “**of interest to study the factors** (endogenous or exogenous) that regulate the synthesis and cleavage of estrogen fatty acid esters since factors influencing the formation and hydrolysis of estrogen fatty acid esters in liver and in extrahepatic target cells may profoundly affect the intensity and duration of estrogen action in the body.” Zhu et al. further states that “**the significance** of this effect on estrogen’s hormonal action **remains to be elucidated.**” Zhu et al. (Carcinogenesis, vol. 19, no. 1, p. 14, emphasis added).

Applicant respectfully submits that a reference which continually suggests and teaches additional research in order to determine the significance, to advance the knowledge and to ascertain the physiological significance of biochemical functions cannot provide a valid basis for a rejection of Applicant’s invention as claimed. There is no explicit or implied teaching,

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suggestion, or motivation for one of ordinary skill in the art to do anything other than more research.

As provided in MPEP 706.02(j) and 2143, first, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; second, there must be a reasonable expectation of success, and finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990); MPEP 2143.01. A statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993); MPEP 2143.01.

Applicant respectfully submits that the application is in condition for allowance. A Notice of Allowance is hereby respectfully requested.

Should the Examiner feel that a telephone conference would advance the prosecution of this application, she is encouraged to contact the undersigned at the telephone number listed below.

The requisite fees of \$290.00 are being charged to Deposit Account No. 50-0694.
Applicant respectfully petitions the Commissioner for any extension of time necessary to render this paper timely. Please charge any fees due or credit any overpayment to Deposit Account No. 50-0694.

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Respectfully submitted,

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